UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/678,016	10/02/2000	Keith P. Wilson	VPI/96-03 DIV2	7947

1473 7590 08/13/2003

FISH & NEAVE
1251 AVENUE OF THE AMERICAS
50TH FLOOR
NEW YORK, NY 10020-1105

EXAMINER
ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
1631	10

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/678,016	WILSON ET AL.	
	Examiner	Art Unit	
	Marianne P. Allen	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 27-62* is/are pending in the application.

4a) Of the above claim(s) *38 and 41-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,27-37,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *23 and 27-62* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's arguments filed 5/20/03 have been fully considered but they are not persuasive.

Election/Restrictions

Newly submitted claims 38 and 41-62 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 38 is directed to a method of identifying an inhibitor. Claims 41-51 are directed to methods of designing a compound or complex. Claims 52-62 are directed to methods of screening a plurality of chemical entities. Each of these methods can be shown to be distinct from the method for evaluating the ability of a chemical entity to associate with a binding pocket as each method has different method steps and/or goals and would require a non-coextensive search (patent and non-patent literature).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 38 and 41-62 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

Claims 37 and 39-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 37 is newly presented and basis is stated to be on pages 29-30 and 32-34. Energy minimization and molecular dynamics are disclosed in the context of docking using known software followed by both energy minimization and molecular dynamics. Basis for these techniques alone and in the absence of docking is not seen.

Claim 39 is newly presented and basis is stated to be in Examples 2-4. Examples 2-4 disclose production of a particular crystal under particular conditions. A specific binding pocket was identified. There is no general disclosure of producing any crystal or molecular complex of IMPDH and/or determining other binding pockets.

Claim 40 indicates that the fitting operation is performed though visual inspection. Basis is stated to be on pages 19 and 29. These portions of the specification indicate that while visual inspection may be the starting point, the process must involve docking chemical entities of interest within the binding pocket using known algorithms. There does not appear to be basis for using visual techniques alone.

Claims 23, 27-37, and 39-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Independent claims 23, 29, and 32 have been amended to be directed to a method for evaluating the ability of a chemical entity to associate with all or any part of a binding pocket defined by given structure coordinates. The steps set forth are to performing a fitting operation

to associate the chemical entity with the binding pocket, quantifying the association, and outputting the quantified association to a suitable output hardware.

The English language definition of the word "evaluate" is considered to mean to determine the significance or degree of association (including no association) within the context of these methods. That is, there must be some determination within the steps of the claim that a particular chemical entity is considered to associate with the binding pocket or not to associate with the binding pocket. First of all, by reciting "fitting operation to associate the chemical entity" the claims indicate that all chemical entities will associate with the binding pocket and thus the claim steps no longer evaluate the ability to associate. The claims are internally inconsistent and/or confusing. In addition, the claim steps recite quantifying alone which does not fulfill the requirement of evaluating. An abstract value in the absence of something to compare it to does not provide an evaluation. Applicant is advised that if the preamble of the claim is amended to be directed to quantifying the association of a chemical entity (or similar language) such a method is considered to lack patentable utility as it produces no information of any value to those of ordinary skill in the art. That is, unless the method discriminates in some fashion between chemical entities that associate and those that do not or between chemical entities that associate better than other chemical entities or that a particular degree of association results in a desired outcome (e.g. inhibition), one of ordinary skill in the art would not know how to use the information produced. As is clear from the prior Office action, the claims have been interpreted by the examiner to intend such a discrimination in view of the recitation of "evaluating" and have not been considered enabled as written in part for these reasons. Applicant is requested to clarify how they are interpreting the limitations of the claims,

particularly with respect to the preamble language and the recitation "fitting operation to associate."

It is noted that the specification does not exemplify the method as claimed that is merely quantifying. Example 6 is prophetic, yet even this example is directed to designing inhibitors which must necessarily associate to the degree necessary to inhibit the biological activity. These prophetic examples indicate the desirability of a lowest-energy bound conformation or molecule strain energy of 10 kcal/mol or less. The entirety of the specification appears to be directed to identifying chemical entities with a particular degree of associating.

As set forth in the prior Office action, the specification defines "associating with" as referring to a condition of proximity between a chemical entity or compound which can be covalent or non-covalent. (See at least page 13, paragraph bridging pages 27-28, and first full paragraph on page 28.) However, the steps of the claims do not have any limitations as to the determining these types of associations with the named amino acid positions and do not appear to require these proximities. The meets and bounds of a "fitting operation" do not appear to be defined in the specification. Applicant was requested to point to the portion of the specification that clarifies what was intended to be encompassed. While applicant pointed to examples of what was intended, applicant did not point to a limiting definition. In the absence of a clear definition, the type of quantification of the results of such an operation is not defined. It is not known from the specification in a general way what type of value the claims require (e.g. estimated interaction energy, conformation energy, etc.) nor what values constitute an association versus a non-association. The specification provides no examples using the structural coordinates of Figure 1 in the method as claimed. No fitting operation is performed

for any chemical entity, no analysis of the results leading to quantification of the association is performed, no output of this quantification is exemplified for the IMPDH binding pocket using any computational means.

Many of applicant's arguments are with respect to limitations not found in the claims (e.g. preferred deformation energies of binding). As such, these arguments are not persuasive.

Claims 23, 27-37, and 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23, 29, and 32 identify particular amino acids that define a binding pocket in the preamble. However, the body of the claim recites "employing...all or part of said structure coordinates... to associate...with said binding pocket." The claims are unclear because the structure coordinates used may be less than those recited in the preamble as defining the whole binding pocket whereas the body of the claim appears to require fitting to the entire binding pocket.

Claim 35 remains confusing in failing to further define the binding pocket of claim 29 clearly. If the claim was intended to require additional structural coordinates to define the binding pocket referred to in the body of claim 29, this should be made clear. The identity of the molecule or complex does not alter the steps of the body of the claim.

Claim 36 remains confusing as claim 32 (upon which claim 36 depends) defines the binding pocket coordinates and it is unclear how this claim modifies these coordinates or the

method claimed. The identity of the molecule or complex does not alter the steps of the body of the claim.

Claim Rejections - 35 USC § 103

Claims 23, 27-37, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohm.

This rejection is maintained for reasons of record as applied to claims 23 and 27-36.

Bohm teaches the computer program LUDI for design of enzyme inhibitors by positioning small molecules (the instant chemical entity) into clefts of protein structures (the instant binding pocket), using particular calculations for fragment fitting to interaction sites (the instant fitting operation and analysis of the results to quantify the association) and outputting the three dimensional representation of the designed molecule in association with the enzyme used as input (which is considered to meet the requirement of step (c) as the resulting molecule is based upon the program calculations). Input for the program is three dimensional structure information.

Bohm teaches at least the energy minimization required by claim 37 and the visual inspection required by claim 40.

The difference between the prior art and the claimed invention is the recited three dimensional structure information. This information is descriptive information stored on or employed by a machine. This information is fed into a known algorithm whose purpose is to compare or modify those data using a series of processing steps that do not impose a change in the processing steps and are thus nonfunctional descriptive material. The claimed invention uses known software to solve a known problem in a conventional manner. The instant specification

acknowledges known prior art computer modeling techniques. Neither the specification nor the claims set forth any special, non-obvious modifications to the known, conventional software and method steps. A method of using a known comparator (e.g. computer modeling techniques known in the prior art to Bohm) for its known purpose to compare data sets does not become nonobvious merely because new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. See *In re Gulack*, 703 F. 2d 1381, 1385 (Fed. Cir. 1983) and MPEP 2106. Applicant is also directed to the Trilateral Project WM4 Report on Comparative Study on Protein 3-dimensional (3-D) Structure Related Claims at http://www.uspto.gov/web/tws/wm4/wm4_3d_report.htm. See in particular discussion regarding case 7, claim 1.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 8:30 am - 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa
August 6, 2003

BRUCE KISLIUK, DIRECTOR
TECHNOLOGY CENTER 1600